UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,410	11/17/2005	Giovanni Paganelli	GRT/4865-17	4581

23117 7590 01/05/2009
NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
GUSSOW, ANNE	
ART UNIT	PAPER NUMBER
1643	
MAIL DATE	DELIVERY MODE
01/05/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/554,410	PAGANELLI ET AL.	
	Examiner	Art Unit	
	ANNE M. GUSSOW	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-14 and 18-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-14 and 18-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/31/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 31, 2008 has been entered.

2. Claims 1, 18, and 23 have been amended.

Claim 29 has been added.

Claims 2 and 15-17 have been canceled.

3. Claims 1, 3-14, and 18-29 are under examination.

4. The following Office Action contains NEW GROUNDS of Rejection.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on October 31, 2008 has been fully considered by the examiner and an initialed copy of the IDS is included with the mailing of this Office Action.

Rejections Maintained/ NEW GROUNDS of Rejection

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The rejection of claims 1, 3-13, 18-28, and newly added claim 29 under 35 U.S.C. 103(a) as being obvious over Goldenberg in view of Cokgor, et al. is maintained.

The response filed October 31, 2008 has been carefully considered but is deemed not to be persuasive. The response states that Cokgor administered radiolabeled antibody by direct injection into spontaneous cysts, into surgically created resection cavities (SCRCs), intrathecally, and into tumors. But delivering a single dose of radiation directly to the tumor, exposed during surgery, or to the anatomical area that contained the tumor after surgical removal of the cancer is disadvantageous because such procedures are logistically complicated and expensive: only a few primary treatment centers have the necessary expertise to implement this type of therapy; the cost of the equipment alone is several million dollars (without even considering the construction costs for building a shielded operating theater to ensure radioprotection for the operators and people in the adjacent rooms), and the specialist staff necessary for implementing the treatment. See page 2, first paragraph, of Applicants' specification.

The intravenous inoculation of the labeled antibody as disclosed in Goldenberg does not present the disadvantages described above, but only a modest amount of antibodies and proteins of the avidin family reach the target after inoculation. See page 3, first paragraph, of Applicants' specification. Also Cokgor teaches that systemically administered radiolabeled monoclonal antibodies (mAbs) have not been effective in the treatment of brain tumors because (1) only small amounts of mAb will cross the blood-brain barrier, (2) there is high interstitial fluid pressure in tumors and surrounding normal tissue, (3) mAb lacks specificity and have less than optimal binding affinity, and (4) the catabolism of radioactive label. The aforementioned are explicit teachings away from combining Goldenberg and Cokgor as proposed in the Office Action (see response pages 8-10).

In response to this argument, nowhere in Cokgor does it discuss the cost or difficult logistics as mentioned by applicant. Further, the base claim (and many of the dependent claims) do not require radioactivity which would render applicant's arguments regarding the expense and safety of Cokgor's method moot. Goldenberg, et al. has administered a biotinylated antibody preparation to ovarian cancer patients followed by avidin three days later (see example 3). This procedure treats a malignant tumor with biotin and avidin reagents.

Regarding applicant's comments on the Cokgor reference, one of ordinary skill in the art would expect the blood brain barrier to exclude many treatment compounds, however, the blood brain barrier does not play a role in a locoregional administration, as Cokgor teaches in the introduction, the basis for their treatment method was to resolve

these transmission issues through administration into tumors or resection cavities directly. Further, although the Cokgor study did not include a relationship between survival and total dose (see discussion page 3871 1st column) one of ordinary skill in the art could envisage an advantage of locoregional administration would be the reduction of dose. Additionally, since the claims do not define the particular solid tumor for treatment, only brain tumors would involve the blood brain barrier, other solid tumors would be more easily treated with the two step method of Goldenberg. Thus, as set forth in the previous office action, one of ordinary skill in the art would be motivated to and have a reasonable expectation of success to administer the first composition of Goldenberg locally as taught by Cokgor and the second composition parenterally as taught by Goldenberg.

Therefore after a fresh consideration of the claims and the evidence provided the rejection is maintained.

8. Claims 1, 3-14, 18-28, and newly added claim 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldenberg (US PG PUB 2001/0006618, published July 5, 2001) in view of Cokgor, et al. (Journal of Clinical Oncology, 2000. Vol. 18, pages 3862-3872) and MacPhee, et al. (US PAT 6,054,122, issued April 25, 2000).

Claim 14 recites a method of treating a patient with a solid tumor, said method comprising: (a) administering intraoperatively via a locoregional route to said patient a first agent endowed with tumor tropism capable of concentrating locally on the tumor or in the vicinity of it and then (b) administering postoperatively via a systemic route a

second anticancer agent with affinity for said first agent whereby increased accumulation of said agent endowed with tumor tropism reduces the amount of said second anticancer agent to be administered, in which said first agent is administered by spray.

Goldenberg teaches a method for treating tumor by injecting a patient with a first agent comprising an avidin- or biotin-conjugated antibody which binds to a marker produced by or associated with the lesion and a second agent comprising either avidin or biotin and a radiolabel (paragraphs 36 and 61). Goldenberg teaches suitable radiolabels to include Yittruim-90 (paragraph 114). Goldenberg teaches dosing the first and second agents 24 hours apart (paragraph 133). Goldenberg teaches the method can be used for treating ovarian tumors (example 3). Goldenberg, et al. do not teach locoregional administration of the first agent by a spray. Goldenberg, et al, do not teach treatment of breast, pancreas, lung, pleural, peritoneal, cervico-facial brain or bladder tumors. These deficiencies are made up for in the teachings of Cokgor, et al and MacPhee, et al.

Cokgor, et al teach administration of radiolabeled 81C6 antibody directly to the surgical resection cavity in patients with malignant gliomas.

MacPhee, et al. teach administration of supplemented tissue sealant (TS) by spraying (column 25 lines 27-44). The TS may be supplemented with growth factors, drugs or antibodies (column 12 lines 19-53).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the cancer treatment agent of

Goldenberg in the administration method as taught by Cokgor, et al. and the spray administration as taught by MacPhee, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the treatment agent of Goldenberg in the administration method of Cokgor, et al. and the spray administration of MacPhee, et al. because Cokgor, et al. teach that systemically administered antibodies are not as effective in the treatment of brain tumors because antibodies do not cross the blood brain barrier well and there is high interstitial fluid pressure in the tumor and surrounding normal tissue. Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the agent of Goldenberg in the administration method of Cokgor, et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow

December 31, 2008

/David J Blanchard/
Primary Examiner, Art Unit 1643